Current Therapy for Demodicosis in Dogs and Cats

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Canine demodicosis

Canine demodicosis is a noncontagious parasitic skin disease caused by an overpopulation of the host-specific follicular mites of the genus Demodex. Most cases of canine demodicosis are caused by *Demodex canis*, although two other species of demodex mites are reported. Localized demodicosis is a common mild and benign self-limiting disease. Generalized demodicosis, in contrast, is a serious and potentially life-threatening disease. Most cases of generalized demodicosis are juvenile in onset and develop in dogs less than 1 year of age.

Etiology

A genetically preprogrammed immunologic defect probably is responsible for juvenile-onset, generalized demodicosis. Immunosuppressive diseases such as Cushing's disease and neoplasia can induce adult-onset canine demodicosis. Glucocorticoids and other immunosuppressive or cytotoxic agents also can induce demodicosis. Marked breed predilections and clustering in litters support a hereditary basis for juvenile-onset generalized demodicosis. Data suggests an autosomal recessive mode of inheritance. The American College of Veterinary Dermatology recommends neutering all dogs who have had generalized demodicosis so that the incidence of the disease is decreased and not perpetuated.

Clinical features

Generalized canine demodicosis is characterized by the progression of multifocal, erythematous, partially alopecic, crusted papules and macules that can lead to plaques. Open draining lesions, crusted plaques, alopecia, and exfoliation are signs of more severe disease. Hyperpigmentation, lichenification, and scarring develop with chronic infection. Secondary bacterial infection with generalized deep folliculitis and furunculosis, occasional cellulitis, and tissue necrosis may contribute greatly to disease severity, morbidity, and mortality. Hairloss may be surprisingly minimal in long-coated breeds with long anagen hair cycles such as the Maltese, Shih Tzu, Lhasa Apso, and Miniature Poodle; this may lead to a decreased index of suspicion for demodicosis.

Diagnosis

Diagnosis is not difficult in most dogs with demodicosis. Skin scrapings or hair plucking readily demonstrate mites. Skin biopsy may be required to rule out demodicosis if the disease is chronic, severely affects the paws, or in the Chinese Shar Pei.

Feline demodicosis

Feline demodicosis is a rare or regional skin disease caused by at least three different species of demodectic mites. Feline superficial demodicosis is a contagious, transmissible frequently pruritic generalized skin disease caused by the surface dwelling mite, *Demodex gatoi*. Feline follicular demodicosis caused by the feline follicular mite, *Demodex cati* resembles Demodex canis infection in dogs.

Feline superficial demodicosis

Feline superficial demodicosis does not have a canine counterpart. It is believed to be rare in most of North America, but is found more commonly in localized enzootic regions of the southern and southeastern U.S.A. Feline superficial demodicosis may be increasing in frequency where modern insect-specific parasiticides that do not kill acarids are used for flea control. Clinical features vary from asymptomatic alopecia to alopecia with variable pruritus and self-trauma. If pruritus is absent, cats can present with diffuse, bilaterally symmetric alopecia, plus or minus scaling, affecting the ventral and lateral trunk and caudal legs. Pruritus, if present, usually is intense leading to erythema, crusting and excoriation.

Skin scrapings may not yield mites or eggs in pruritic cats since excessive grooming can remove surface-living mites. Skin scrapings of non-pruritic cats may yield large numbers of mites.

Feline follicular demodicosis

Feline follicular demodicosis due to *D. cati* is rare and may present as either localized or generalized follicular demodicosis. Feline localized demodicosis, similar to canine localized demodicosis, is a mild and may be a self-limiting disease. Feline generalized follicular demodicosis due to D. cati, similar to canine generalized demodicosis, seems to require diminished immune response. Immunosuppressive diseases such as feline immunodeficiency virus infection (FIV), feline leukemia virus (FeLV), diabetes mellitus, hyperglucocorticoidism, and neoplasia may initiate feline generalized follicular demodicosis. Feline generalized follicular demodicosis is unusally a less severe disease than canine generalized demodicosis. Predominantly asymptomatic and subtle erythema with variable alopecia, scaling, and crusting may be seen. Lesions most commonly affect the face, neck, trunk, or extremities. Secondary pyoderma is rare in the feline compared to the canine contributing to less morbidity. Systemic signs referable to underlying immunosuppressive systemic diseases may be noted.

Canine generalized demodicosis – Overview of treatment

Treatment of canine generalized demodicosis remains challenging. There is no treatment for generalized demodicosis that is 100% effective, even though multiple options currently are available. However, most dogs can be successfully managed long-term. Glucocorticoid usage must be avoided. Secondary deep pyoderma usually coexists with canine generalized demodicosis and must be treated aggressively. Antibiotics such as cephalexin, enrofloxacin, marbofloxacin, and clavulanic acid-potentiated amoxicillin are used most commonly and usually are continued for a minimum of 8 weeks. Selection in many cases may need to be made on culture and sensitivity especially when methicillin resistant infections are suspected.

Topical adjunctive therapy is beneficial. Antibacterial and follicular flushing shampoos containing benzoyl peroxide aid greatly in management of both demodicosis and secondary pyoderma. Chlorhexidine based products can also be effective.

Amitraz

Amitraz (Mitaban®, Pfizer) is an FDA approved treatment for generalized canine demodicosis. Before amitraz rinses, all medium and long-coated dogs should be clipped and the hair kept short throughout therapy. Clipping plus benzoyl peroxide-containing shampoos afford better penetration of the dipping solution. Mitaban is diluted according to label directions in the USA (0.025% solution) and applied every 2 weeks. A stronger amitraz solution (0.050% solution) has been used on a weekly basis routinely in Germany, Australia and elsewhere. Using evidence-based medicine, good evidence is available for the efficacy of amitraz rinses (0.025-0.05% solutions) used every 1 or 2 weeks. Amitraz rinsing should be performed either outdoors or in an open garage. Rubber gloves should be worn by the applier. Amitraz is an MAO inhibitor and should not be used by anyone taking other MAO inhibiting drugs. Continuous rinsing of the entire dog with the dipping solution and soaking of the feet in the solution should continue for 15 minutes. The dog should be kept as dry as possible (avoiding of walking on wet lawns) between rinses. Amitraz rinses should be continued every 2 weeks until multiple negative skin scrapings and hair plucks (no adults, larvae, or eggs) are achieved. After negative scrapings and hair plucks have been achieved, 3 additional rinses should be performed. After 3 additional rinses, reexamination should include 6 to 10 skin scrapings and hair plucks before rinses are terminated. It is not uncommon for 10 to 15 rinses to be required before negative scrapings are achieved. Side effects of amitraz therapy include lethargy, weakness, ataxia, hyperglycemia, polyuria, hypothermia, and bradycardia. Atipamezole (Antisedan) (50 µg/kg, IM) and yohimbine (0.11 mg/kg, IV; 0.25 mg/kg, IM) may be used as a pretreatment in dogs with previous reactions to amitraz or can be used as antidotes for toxicity. Resistant cases may require off label application of amitraz rinses weekly rather than biweekly. In cases that are controlled but not cured, a maintenance program of every 1 to 2 week rinses may be instituted to keep mite numbers low and clinical signs minimized. Dogs with adult onset demodicosis and concurrent immunosuppressive diseases frequently require extended therapy regimens.

Metaflumizone and amitraz

A spot-on formulation containing metaflumizone plus amitraz (ProMeris®/ProMeris Duo® for dogs, Pfizer) has been evaluated in 3 different studies. In the first study by Fourie sixteen dogs infested with *Demodex* sp. were treated with 20 mg kg^{-1} of both metaflumizone and amitraz. Two groups differed in interval of treatment, 28 or 14 days. *Demodex* dogs were treated on four or six occasions. Treatment at 28-day or 14-day intervals resulted in a reduction in mite numbers of 94% and 99%, respectively and an improvement in clinical signs. No side effects were reported. In the second study by Heany 14 mixed breed dogs, 8 male and 6 female with clinical signs of generalized demdocosis were treated with a mean age = 2.25 yrs and a range of >6 months – 5 yrs. Only one dog was less than 1 year of age. Dogs were housed at the shelter until adopted into private homes. All dogs remained in the study through the Day 56 evaluation. Two dogs dropped out at Day 84. One month after the 3rd treatment. 64% (9 of 14 dogs) achieved clinical cure. No side effects were reported. In a 3rd study performed by the author 24 dogs with juvenile (n = 13) or adult onset (n=11) generalized demodicosis. Case selection included option for initial therapy by owner preference (3/24), undesirable side effects of previous treatment (6/24) or lack of efficacy of previous treatments (15/24). All were treated with a minimum dose rate (20mg $kg^{-1}$of metaflumizone and amitraz, 0.133ml/kg^{-1}) at a 14 day interval until 2 consecutive negative skin scrapings were obtained. Cases were evaluated every 30 days. The treatment times ranged from 90 – 180 days. The results were based on reduction of mite numbers. A grading score was assigned as excellent if no mites were identified for 60 days (2 negative scrapings), good if 75% reduction, fair if 50% reduction and poor if no change in mites numbers within 90 days. Other antimicrobial therapies were allowed throughout the study. Cases were monitored for side effects and complications. Of the 13 juvenile onset cases, 12/13 (92.3%) had excellent results and 1/13 (7.7%) had poor results. In the 11 adult onset cases, 5/11 (45.4%) had excellent results, 3/11 (27.3%) had good results and 3/11 (27.3%) had poor results. Side effects included a pemphigus foliaceus-like pustular eruption (1), vomiting (1), diarrhea (2), transient lethargy (2) and product odor (7). Efficacy was comparable to other products and is an approved alternative to other treatment options. The product is currently off the market and it is not likely it will be brought back due to the concern for the pemphigus foliaceus like drug eruptions.

Ivermectin
Ivermectin (Ivomec®, Merial; DVMectin®, IVX/DVM) is a commonly used, but non-approved, treatment for generalized canine demodicosis. Ivermectin is given daily per os at a dosage between 400 and 600 micrograms/kg daily. High dose ivermectin is the most efficacious and cost-effective treatment for generalized demodicosis. Using evidence-based medicine, good evidence is available for the efficacy of ivermectin given per os (300-600 micrograms/kg daily). Severe adverse reactions to ivermectin are ususally limited to dogs that are homozygous for the dangerous mutant ABCB1-1Δ (formerly MDR1) allele leading to neurotoxicity Collies are particularly sensitive with over 75% of Collies being either carriers or homozygous for the dangerous mutant ABCB1-1Δ (formerly MDR1) allele. Information on testing for this mutation can be found at http://www.vetmed.wsu.edu/depts-vcpl/. Other herding breeds such as the Shetland Sheepdog, Australian Shepherd, and Border Collie also may be at increased risk for toxicity. However, idiosyncratic toxicity may be seen in any breed. Similar to the monitoring of efficacy used with amitraz topical therapy, dogs are reevaluated monthly until multiple negative skin scrapings and hair plucks (no adults, larvae, or eggs) are achieved. After negative scrapings and hair plucks have been achieved, therapy is continued for an additional 2 months. Two months beyond the last negative skin scraping and hair pluck, reexamination should include multiple skin scrapings and hair plucks before therapy is terminated. It is not uncommon for 4 to 6 months of therapy to be required before negative scrapings are achieved.

Milbemycin oxime
Milbemycin oxime (Interceptor®, Novartis) is another commonly used but non-approved, treatment for generalized canine demodicosis. It is used less frequently than ivermectin, as milbemycin therapy is considerably more expensive. However, milbemycin is a very safe avermectin for the treatment of demodicosis and can be used in herding breeds such as the Collie. Milbemycin also is recommended for small dogs based on cost. Milbemycin is given daily per os at a dosage of 2 mg/kg daily. Using evidence-based medicine, good evidence is available for the efficacy of milbemycin given per os (2 mg/kg daily). Milbemycin therapy is considerably less toxic than ivermectin therapy. Side effects are rare, but at high dosages may include vomiting, stupor, trembling, and ataxia. Identical to the monitoring of efficacy used with ivermectin oral therapy, dogs are reevaluated monthly until multiple negative skin scrapings and hair plucks (no adults, larvae, or eggs) are achieved. After negative scrapings and hair plucks have been achieved, therapy is continued for an additional 2 months. Two months beyond the last negative skin scraping and hair pluck, reexamination should include multiple skin scrapings and hair plucks before therapy is terminated. It is not uncommon for 4 to 6 months of therapy to be required before negative scrapings are achieved.

Moxidectin
Moxidectin (ProHeart 6®, Fort Dodge), currently not available in the USA, also has been used as another non-approved, treatment for generalized canine demodicosis. Evidence-based medicine indicates good evidence for the efficacy of moxidectin given per os (400 micrograms/kg daily). Imidacloprid & Moxidectin (Advantage Multi®, Advocate®, Bayer) has a label claim for demodicosis at monthly application, however current studies suggest greater efficacy if used on a weekly to bimonthly basis.

Doramectin
Doramectin (Dectomax®, Pfizer), not available in the U.S. has been used at 300 micrograms/kg/day orally successfully in Australia, New Zealand & Japan, side effects similar to those seen with ivermectin.

Feline demodicosis – Overview of treatment
There is no FDA approved treatment for feline demodicosis. Because of the sensitivity of cats to many of the miticidal therapies, lime sulfur should be utilized whenever possible because of its larger margin of safety.

Lime sulfur
Lym dip®, (IVX/DVM Pharmaceuticals) miticidial mechanism of action of lime sulfur is unknown. In human dermatology, lime sulfur's efficacy against mites is believed to be due to a combination its keratolytic effect and the formation of miticidal products, such as hydrogen sulfide and polythionic acid. Lime sulfur dip is a very safe topical medication. It can cause gastrointestinal signs in cats, so it is recommended that after dipping they wear an Elizabethan collar until dry. When the head needs to be a treated, the area should be sponged, and the eyes and mouth avoided. The main disadvantage of lime sulfur dip is the undesirable odor of "rotten eggs". This topical is also capable of tarnishing jewelry and staining wood and clothing. Owners of light colored animals should be warned that their animal's fur will temporarily be stained yellow. Lastly, this product can be drying and irritating, so it can be helpful to use a moisturizing shampoo prior to the dip.

Lime sulfur dip is the recommended treatment for feline demodex caused by *Demodex gatoi.* Weekly dips for 6 weeks are recommended, using a 3.1% concentration (4 ounces of dip per gallon of water). When trial treatment for cats with suspect demodex is performed, have the owner commit to at least three lime sulfur dips. If the cat is showing significant improvement after three dips, finish all six treatments. If the cat is unresponsive, evaluate for other appropriate differentials.

Although it is not clear why lime sulfur is effective against a follicular mite, there are several reports of cats with Demodex cati infection responding to this treatment and the author recommends using this treatment prior to amitraz dips or other mitcidal therapies.

Ivermectin

Ivermectin (Ivomec®, Merial) can be used at a dose of 0.3mg/kg orally once weekly for four consecutive treatments . The margin of safety of ivermectin appears to be smaller in cats than in dogs, so other treatments should be utilized first. There are anecdotal reports of every other day dosing of ivermectin being a more successful and equally safe treatment.

Amitraz

Amitraz (Mitaban®, Pfizer)is not licensed for use in cats, and because of potential side effects is not recommended by the manufacturer or the author for use. Side effects of amitraz in cats include sedation, anorexia, lethargy, hypersalivation and diarrhea. There are several reports in the literature of the medication being effective in the treatment of feline demodex infections when 0.0125%-0.025% solution is used every 5-7 days for 4-6 weeks. See canine demodex section for more safety information about this drug.

Referenes

Beale, K.M. Contagion and occult demodicosis in a family of 2 cats. 14th Proceedings of the AAVD/ACVD Meeting, San Antonio, Texas, 1998, p 99 (abstract).

Mealey KL, Bentjen SA & Waiting DK. Frequency of the mutant MDR1 allele associated with ivermectin sensitivity in a sample population of collies from northwestern United States. Am J Vet Res 2002, 63: 479-481.

Morris DO, Beale KM. Feline demodicosis. In Bonagura JD (ed): Kirk's Current Veterinary Therapy XIII, Philadelphia, WB Saunders Company, 2000, p 580.

Mueller RS. Treatment protocols for demodicosis: An evidence-based review. Vet Derm 2004 15:75-89.

Gross TL, Ihrke PJ, Walder EJ, Affolter VK: Skin Diseases of the Dog and Cat: Clinical and Histopathologic Diagnosis. Blackwell, Oxford, pp 222-225, 442-448, 464-466, 2005.

Fourie LJ, Kok DJ, du Plessis A, Rugg D: Efficacy of a novel formulation of metametaflumizone plus amitraz for the treatment of demodectic mange in dogs. Vet Parasitology 2007, 150, 268-274.

Mealey KL, Meurs KM: Breed distribution of the ABCB1-1Δ (multidrug sensitivity) polymorphism among dogs undergoing ABCB1 genotyping. JAVMA 233:921-924, 2008.

Rosenkrantz, WR, Efficacy of metaflumizone plus amitraz for treatment of juvenile and adult onset generalized demodicosis in dogs: pilot study of 24 dogs, North American Dermatology Forum, Savannah, Georgia, 2009.

Dryden, M.W. and P.A. Payne, Preventing parasites in cats. Vet Ther, 2005. 6(3): p. 260-7.